REMARKS

Claim Rejections – 35 USC §103

Claims 3, 5, and 7 and 9 have been rejected as being unpatentable over Jindrich et al. in view of DeRosch et al.

The following arguments will show that Jindrich et al. and DeRosch et al. in combination do not teach or suggest the invention as claimed in claim 5 to a person of ordinary skill in the art. Neither do they motivate a person of ordinary skill in the art to derive the claimed invention.

It is submitted that a person of ordinary skill in the art would not have combined the two references because there is no teaching, suggestion or reason to do so in both of the references.

Jindrich et al. labeled the partially methylated β-cyclodextrin with ^{13}C to investigate the regioselectivity of alkylation (the substituents) of cyclodextrin (β-CD):

> To determine the distribution of substituents among the 2-,3-, and 6-, positions, we did methylation experiments involving isotopic enrichment by ^{13}C. In each of these experiments we sued the same amount of 13C-enriched dimethyl sulfate, either as furnished or after dilution with nonenriched reagent ot methylate β-CD....
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> (page 76, lines 6 to 3 from the bottom)

That is, the experiments were conducted specifically to understand the regioselectivity of alkylation of cyclodextrin (see also Table 2 on page 77) by alkyating ^{13}C-enriched dimethyl sulfate to cyclodextrins to create ^{13}C-methyl-cyclodextrin. It does not teach or suggest indiscriminately labeling any form of modified cyclodextrins; and it does not teach or suggest labeling unmodified cyclodextrins because that would not serve to understand the regioselectivity of alkylation of cyclodextrin.

In DeRosch et al., modified and unmodified cyclodextrin were put into the radiopharmaceutical kit to stabilize the components of the kit:

> Because modified or unmodified cyclodextrins have a hydrophobic interior, their use is especially attractive for stabilization of the organic ligands included in a radiopharmaceutical kit. The addition of modified or unmodified cyclodextrins to a kit formulation which includes such organic compounds acts to inhibit the disadvantageous oxidation and/or volatilization.
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> (Column 3, lines 6 to 12)

Cyclodextrins whether modified or unmodified are not labeled themselves in DeRosch et al. Rather, because radiopharmaceuticals are designed to contain radioactive metals such as Tc-99m, Re-186, and Re-188 (see column 2, lines 11 to 21), labeling cyclodextrins with carbon 13 would be totally unnecessary and may even interfere with the proper and intended utilization of the radiopharmacuetical kits.

Therefore, for the foregoing reasons, neither Jindrich et al. nor DeRosch et al. offer any teaching, suggestion, motivation, or desirability to combine one with the other. There is simply no reason for a person of ordinary skill in the art to do so.

Furthermore, even assuming *arugendo* that the cited reference are combinable, Applicants submit that they still would not render the claimed invention prima facie obvious for the following reasons.

The mere fact that references <u>can</u> be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. *In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990).

As stated previously, in Jindrich et al. the cyclodextrin was alkylated with ^{13}C-enriched dimethyl sulfate to create ^{13}C-methyl-cyclodextrin with the sole purpose of studying the

regioselectivity of alkylation of cyclodextrin. In DeRosch et al, radiopharmaceutical kits are designed to contain radioactive metals such as Tc-99m, Re-186, and Re-188 (see column 2, lines 11 to 21), and cyclodextrins whether modified or unmodified are not labeled themselves, and therefore, labeling cyclodextrins with carbon 13 would be totally unnecessary and may even interfere with the proper and intended utilization of the radiopharmacuetical kits. Because Jindrich et al.' study is to investigate the regioselectivity of alkylation of cyclodextrin on the one hand, and DeRosch et al.'s purpose of using modified or unmodified cyclodextrin (which is not and does not need to be labeled) is to stabilize the components of the radiopharmaceutrical kits, on the other hand, the nature of the problem to be solved as a whole between the two is completely different form each other. Clearly, both references do not suggest any desirability of the combination, and the references, even if they are combined, do not render the claimed invention obvious.

Moreover, even assuming *arguendo* that DeRosch et al.'s modified or unmodified cyclodextrins are ^{13}C-labled, based on the teaching of Jindrich et al., the resultant labeled cyclodextrins would still not render the claimed invention obvious.

DeRosch et al. teaches the following modified or unmodified cyclodextrins:

> The modified or unmodified cyclodextrin must be pharmaceutically acceptable and may be selected from α-cyclodextrins, β-cyclodextrins, γ-cyclodextrins, and combinations thereof. Particular α-cyclodextrins which may be used in the kits according to the present invention are hydroxypropyl-α-cyclodextrin, and hydroxyethyl-α-cyclodextrin.
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> Particular β-cyclodextrins which may be used in the kits according to the present invention are hydroxypropyl-β-cyclodextrin, carboxymethyl-β-cyclodextrin, dihydroxypropyl-β-cyclodextrin, hydroxyethyl-β-cyclodextrin, 2,6-di-O-methyl-β-cyclodextrin, and sulfated-β-cyclodextrin. Preferably, hydroxypropyl-α-cyclodextrin is added to the kits according to the present invention.
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> Particular γ-cyclodextrins which may be used in the kits according to the present invention are hydroxypropyl-γ-cyclodextrin, dihydroxypropyl-γ-cyclodextrin, hydroxyethyl-γ-cyclodextrin, and sulfated-γ-cyclodextrin.
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> (Column 3, lines 21 to 40)

Even assuming that these modified and unmodified cyclodextrins (hydroxypropyl-α-cyclodextrin, hydroxyethyl-α-cyclodextrin, hydroxypropyl-β-cyclodextrin, carboxymethyl-β-cyclodextrin, dihydroxypropyl-β-cyclodextrin, hydroxyethyl-β-cyclodextrin, 2,6-di-O-methyl-β-cyclodextrin, sulfated-β-cyclodextrin hydroxypropyl-γ-cyclodextrin, dihydroxypropyl-γ-cyclodextrin, hydroxyethyl-γ-cyclodextrin, and sulfated-γ-cyclodextrin) have the attached group labeled with ^{13}C, they would still not be part of the claimed invention because the modified groups in claim 5 as amended do not include any ^{13}C-labeled alkyl, alkoxyl, or sulfuryl group. A person of ordinary skill in the art would not have found the claimed invention obvious from the cited references.

For the foregoing reasons, all pending claims are unobvious over the prior art and believed to be allowable. Applicants respectfully request reconsideration of the pending claims.

Please apply any charges, if necessary, or credits to deposit account 06-1050.

Respectfully submitted,

Date: 8/25/03

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